

In re of Appln. No. 09/297,668

IN THE CLAIMS

1-143 (Cancelled)

144 (Currently Amended). A method of identifying and producing a peptide which interacts with a ligand which interacts with a discontinuous epitope of a single biological unit consisting of a protein or consisting of two or more proteins which interact to form a complex, the method comprising:

- (a) providing a plurality of DNA fragments, ~~which~~ consisting of fragments, each of which appears ~~appear in a DNA sequence which that~~ encodes ~~said the~~ single biological unit;
- (b) creating a library consisting of oligonucleotides from said plurality of DNA fragments, each said oligonucleotide comprising at least two of said fragments, said fragments being randomly ligated;
- (c) inserting each of said oligonucleotides from said library of oligonucleotides into an expression system;
- (d) causing the peptides encoded by said oligonucleotides to be expressed;
- (e) screening the expressed peptides for interaction with a ligand that interacts with a

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discontinuous epitope of said single biological unit;

(f) identifying any peptide which so interacts; and

(g) producing any peptide so identified.

145 (Previously Added). A method in accordance with claim 144, wherein said procedure of (a) comprises cutting said DNA sequence to form said plurality of DNA fragments.

146 (Previously Added). A method in accordance with claim 145, wherein said cutting is accomplished enzymatically.

147 (Previously Added). A method in accordance with claim 145, wherein said cutting is accomplished mechanically.

148 (Previously Added). A method in accordance with claim 144, wherein said procedure of (a) comprises synthesizing said plurality of DNA fragments.

149 (Previously Added). A method in accordance with claim 144, wherein said procedure of (b) comprises randomly ligating said plurality of DNA fragments to form at least one ligated fragment and at least partially digesting said at least one ligated fragment to form said library of oligonucleotides.

150 (Previously Added). A method in accordance with claim 144, wherein said expression system comprises a plurality of bacteria and said procedure of (c) comprises

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inserting one of said library of oligonucleotides into each of said plurality of bacteria.

151 (Previously Added). A method in accordance with claim 144, wherein said expression system comprises a plurality of phages and said procedure of (c) comprises inserting one of said library of oligonucleotides into each of said plurality of phages.

152 (Previously Added). A method in accordance with claim 151, wherein said oligonucleotides are inserted into said phages by cloning said oligonucleotides into phage genes coding for a coat protein.

153 (Previously Added). A method in accordance with claim 152, wherein said phages are filamentous phages and said coat protein is pIII or pVIII.

154 (Previously Added). A method in accordance with claim 144, wherein said expression system comprises an eukaryotic expression system and said procedure of (c) comprises inserting said library of oligonucleotides into eukaryotic expression vectors and inserting said vectors into said eukaryotic expression system.

155 (Previously Added). A method in accordance with claim 144, wherein said single biological unit is a protein.

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156 (Previously Added). A method in accordance with claim 144, wherein said single biological unit is two or more proteins which interact to form a complex.

157 (Previously Added/Currently Withdrawn). A method of vaccinating a subject against an organism, comprising placing a product produced in accordance with the method of claim 144 into a vaccine carrier and administering said product and vaccine carrier to the subject.

158 (Currently Amended/Currently Withdrawn). A library consisting of a plurality of peptides, each of which comprises at least two peptide fragments, each said fragment appearing in the amino acid sequence of a single biological unit, said fragments being randomly ligated to form said peptides, wherein said single biological unit consists of a protein or consists of two or more proteins which interact to form a complex.

159 (Currently Amended). A method of preparing a library of peptides which can be screened to find peptides ~~which that~~ interact with ligands which interact with discontinuous epitopes of a single biological unit consisting of a protein or consisting of two or more proteins which interact to form a complex, comprising:

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(a) providing a plurality of DNA fragments, ~~which~~
consisting of fragments, each of which appears ~~appear~~ in a DNA
sequence ~~which that~~ encodes said the single biological unit;

(b) creating a library consisting of
oligonucleotides from said plurality of DNA fragments, each
said oligonucleotide comprising at least two of said
fragments, said fragments being randomly ligated;

(c) inserting each of said oligonucleotides from
said library of oligonucleotides into an expression system;
and

(d) causing the peptides encoded by said
oligonucleotides to be expressed, thereby preparing a library
of peptides.

160 (Previously Added). A method in accordance with
claim 159, wherein said procedure of (a) comprises cutting
said DNA sequence to form said plurality of DNA fragments.

161 (Previously Added). A method in accordance with
claim 160, wherein said cutting is accomplished enzymatically.

162 (Previously Added). A method in accordance with
claim 160, wherein said cutting is accomplished mechanically.

163 (Previously Added). A method in accordance with
claim 159, wherein said procedure of (b) comprises randomly
ligating said plurality of DNA fragments to form at least one
ligated fragment and at least partially digesting said at

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least one ligated fragment to form said library of oligonucleotides.

164 (Previously Added). A method in accordance with claim 159, wherein said expression system comprises a plurality of bacteria and said procedure of (c) comprises inserting one of said library of oligonucleotides into each of said plurality of bacteria.

165 (Previously Added). A method in accordance with claim 159, wherein said expression system comprises a plurality of phages and said procedure of (c) comprises inserting one of said library of oligonucleotides into each of said plurality of phages.

166 (Previously Added). A method in accordance with claim 165, wherein said oligonucleotides are inserted into said phages by cloning said oligonucleotides into phage genes coding for a coat protein.

167 (Previously Added). A method in accordance with claim 166, wherein said phages are filamentous phages and said coat protein is pIII or pVIII.

168 (Previously Added). A method in accordance with claim 159, wherein said expression system comprises an eukaryotic expression system and said procedure of (c) comprises inserting said library of oligonucleotides into

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eukaryotic expression vectors and inserting said vectors into said eukaryotic expression system.

169 (Previously Added). A method in accordance with claim 159, wherein said single biological unit is a protein.

170 (Previously Added). A method in accordance with claim 159, wherein said single biological unit is two or more proteins which interact to form a complex.

171 (Currently Amended/Currently Withdrawn). A method of identifying and producing an oligonucleotide which interacts with a ligand which interacts with a discontinuous epitope of a single biological DNA or RNA unit consisting of a telomere, a tRNA or a ribozyme, the method comprising:

- (a) providing a plurality of DNA fragments, which consisting of fragments, each of which appears appear in a DNA sequence of a single biological DNA unit or correspond to an RNA sequence of a single biological RNA unit;
- (b) creating a library consisting of oligonucleotides from said plurality of DNA fragments, each said oligonucleotide comprising at least two of said fragments, said fragments being randomly ligated;
- (c) if the biological unit is an RNA unit, transcribing the DNA of each of said

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oligonucleotides from said library of
oligonucleotides to RNA to form an RNA
oligonucleotide library;

- (d) screening the oligonucleotide library for
interaction with a ligand that interacts with a
discontinuous epitope of said single biological
unit;
- (e) identifying any oligonucleotide which so
interacts; and
- (f) producing any oligonucleotide so identified.

172 (Previously Added/Currently Withdrawn). A
method in accordance with claim 171, wherein said single
biological unit is a telomere.

173 (Previously Added/Currently Withdrawn). A
method in accordance with claim 171, wherein said single
biological unit is a tRNA.

174 (Previously Added/Currently Withdrawn). A
method in accordance with claim 171, wherein said single
biological unit is a ribozyme.

175 (Currently Amended/Currently Withdrawn). A
method of preparing a library of oligonucleotides which can be
screened to find oligonucleotides which interact with ligands
~~which~~ that interact with discontinuous epitopes of a single

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oligonucleotides, wherein said single biological unit consists of a telomere, a tRNA or a ribozyme.

177 (Previously Added). A method in accordance with claim 144, wherein each of said DNA fragments of (a) has a size of about 50 to about 150 base pairs.

178 (Previously Added/Currently Withdrawn). A library of peptides in accordance with claim 158, wherein each of said peptide fragments has a size of about 17 to about 50 residues.

179 (Previously Added). A method in accordance with claim 159, wherein each of said DNA fragments of (a) has a size of about 50 to about 150 base pairs.

180 (Previously Added/Currently Withdrawn). A method in accordance with claim 171, wherein each of said DNA fragments of (a) has a size of about 50 to about 150 base pairs.

181 (Previously Added/Currently Withdrawn). A method in accordance with claim 175, wherein each of said DNA fragments of (a) has a size of about 50 to about 150 base pairs.

182 (Previously Added/Currently Withdrawn). A library of oligonucleotides in accordance with claim 176, wherein each of said DNA fragments has a size of about 50 to about 150 base pairs.